

REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claims 1, 3-6, 12-15 and 18 are pending in this application.

By this Amendment, claim 1 is amended to recite that Ar is optionally substituted with 1 to 5 substituent(s) selected from the group consisting of groups (1) – (34), ring A is benzene and Xa is a bond, and claim 1 is amended to remove the proviso which excluded the four compounds. Support for the specific substituents (1) – (34) can be found on page 16, line 34 – page 19, line 7 of the specification.

Claims 3, 13 and 14 are amended in accordance with the amendments to claim 1.

Claims 4, 5 and 18 are cancelled without prejudice or disclaimer.

I. Claim Objections

The Examiner objects to claim 1 for containing a proviso. By this Amendment, the proviso is deleted, overcoming the objection.

The Examiner objects to claim 5 as redundant. Claim 5 is cancelled, rendering the objection moot.

II. Claim Rejection Under 35 U.S.C. § 102

The Examiner rejects claims 1, 3, 5, 6, 12-15 and 18 under 35 U.S.C. § 102(e) as being anticipated by Bratton et al. (US 7,244,763) and Auerbach et al. (US 6,875,780).

Claims 5 and 18 are cancelled, rendering their rejection moot. Claim 1 is amended to recite that Xa is a bond, and the compound depicted on page 3 of the Office Action does not include this feature. Therefore, claim 1 is not anticipated by Bratton et al. or Auerbach et al.

Claims 3, 6 and 12-15 depend from claim 1, and thus also are not anticipated by either reference.

III. Claim Rejection Under 35 U.S.C. § 103

The Examiner rejects claims 1, 3-6, 12-15 and 18 under 35 U.S.C. § 103(a) as being unpatentable over Bratton et al. and Auerbach et al. By this Amendment, claims 5 and 18 are cancelled, rendering their rejection moot. As for the remaining claims, Applicants respectfully traverse the rejection.

(1) The compounds of amended claim 1 have a structure wherein a benzene ring as ring A is directly bonded to the cyclic Ar group, and ring A is bonded via methyleneoxy or dimethyleneoxy to a bicyclic non-aromatic ring having a $R^1\text{COCH}_2$ group at a specific position. This chemical structure is clearly different from that of the compounds of the cited references. The cited references do not teach or suggest the chemical structure of the compounds of the present invention. Therefore, claim 1 would not have been obvious over the references for this reason alone.

(2) The cited references disclose the activity data of the compounds of Example 10, Example 21 and Example 31, where the intensity is $\text{Ex. 10} < \text{Ex. 21} < \text{Ex. 31}$. By comparing the chemical structures of these three compounds and that of the compounds of the present invention, Ex. 10, having the lowest activity, is most similar to the compounds of the present invention, and Ex. 31, having the highest activity, is least similar to the compounds of the present invention.

Therefore, one of ordinary skill in the art would expect compounds similar to Ex. 10 to have lower activity, and compounds similar to Ex. 31 to have higher activity. This would suggest to one of ordinary skill in the art that making the compounds of claim 1 would have decreased activity, because they are closer in chemical structure to Ex. 10 of the cited references. Therefore, one of ordinary skill in the art would not have been motivated to prepare compounds of Ex. 10, but rather those of Example 31. Accordingly, the cited references teach away from the compounds of claim 1.

The activity data of Ex. 10, Ex. 21 and Ex. 31 is as follows:

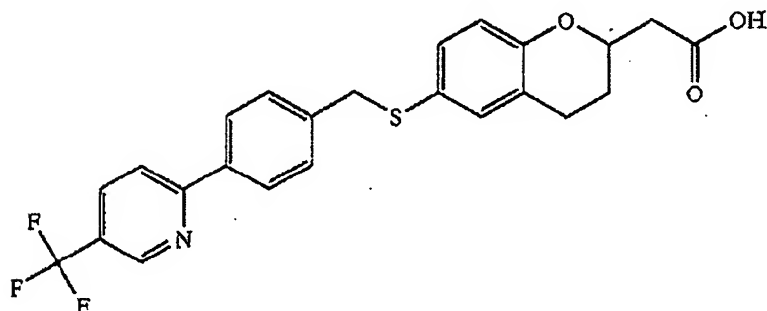
[Test A] Ex. 10: $\text{EC}_{50\beta} = 6660 \text{ nM}$; Ex. 21: $\text{EC}_{50\beta} = 303 \text{ nM}$ (the lower value shows a higher activity).

[Test B] Ex. 21: $\text{IC}_{50\beta} = 449 \text{ nM}$; Ex. 31: $\text{IC}_{50\beta} = 6.8 \text{ nM}$ (the lower value shows a higher activity).

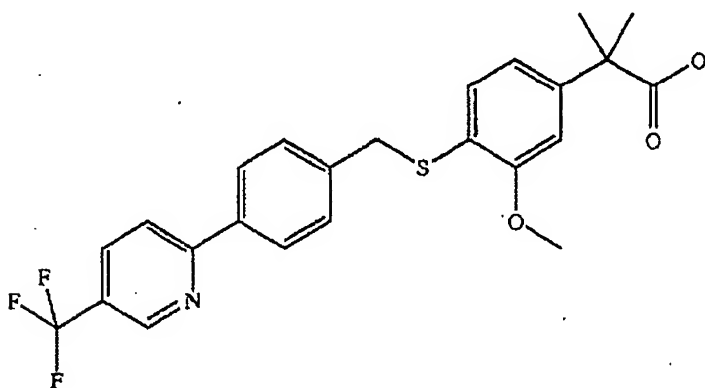
See US 6,875,780 at cols. 137-138 and US 7,244,763 at cols. 144-145, showing the same data.

The chemical structures of Ex. 10, Ex. 21 and Ex. 31 are as follows:

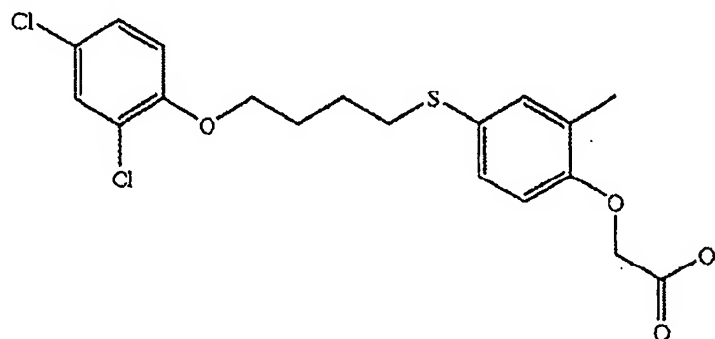
Ex. 10



Ex. 21



Ex. 31



(3) The cited references disclose compounds influential on PPAR activity. On the other hand, the compounds of the present invention have GPR40 agonist activity. As discussed in Applicants' previous remarks, and as shown in the Declaration under 37 CFR 1.132 filed on October 31, 2008, the present invention aims at obtaining a novel compound, particularly having a GPR40 modulating activity, from among the compounds having a treatment effect on diabetes. It has been reported that GPR40 is one of the G protein-coupled membrane receptors frequently

expressed in pancreatic β -cells and acts as a receptor of long-chain free fatty acid, and free fatty acid is promoted via GPR40 insulin secretion from the pancreatic β -cell. On the other hand, as for PPAR (particularly γ related to diabetes) noted by the cited compound, it has been reported that it promotes insulin sensitivity in a tissue. Therefore, GPR40 modulating activity and PPAR modulating activity are different in the point of action in the treatment of diabetes.

Applicants take the position that it would not have been conceivable to those of ordinary skill in the art to prepare the compounds of the present invention having a GPR40 agonistic activity from the cited compound having PPAR agonist activity.

Moreover, as can be seen from the Declaration, a compound having a GPR40 agonistic activity but not having a PPAR modulating activity exists. Such finding teaches that a GPR40 modulating activity and a PPAR modulating activity are not parallel. In other words, even those of ordinary skill in the art would not consider modifying a compound (the cited compound) having a PPAR modulating activity in order to afford a compound having a GPR40 modulating activity.

Therefore, the compounds of claim 1 would not have been obvious to those of ordinary skill in the art over Bratton et al. and Auerbach et al. Claims 3, 6 and 12-15 depend directly from claim 1, and thus also would not have been obvious over the references.

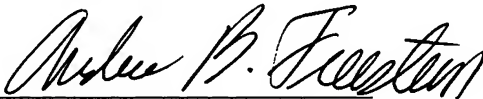
IV. Conclusion

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are earnestly solicited.

Should the Examiner find that anything further would be desirable in order to place the application in better condition for allowance, he is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,

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